

Original
article

Women with recurrent vaginal candidosis have normal peripheral blood B and T lymphocyte subset levels

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Objective: To compare the B and T lymphocyte subset levels of otherwise healthy women suffering from frequently recurrent vaginal candidosis with a healthy control group.

Subjects: 26 unselected otherwise healthy women of reproductive age with at least four attacks of vaginal candidosis in the past year and more than three vaginal isolates of a moderate or heavy growth of *Candida albicans*. Controls were 26 patients or clinical and laboratory staff (asymptomatic for genital infection) matched for time of day and age within 5 years. Only three patients accepted an HIV test. All proved HIV negative. No controls were tested.

Main outcome measures: T lymphocyte subsets (CD4 and 8) and B lymphocytes (CD 19) as estimated from the total lymphocyte count and flow cytometry.

Results: No statistically significant difference between patients and controls.

Conclusion: No significant difference was found between patients and controls in levels of lymphocyte subsets.

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Keywords: candidosis; T lymphocytes; B lymphocytes

Introduction

A majority of women will get an attack of vaginal candidosis (VC) at some time in their life and for most this is an occasional nuisance. In contrast, a few otherwise healthy women suffer from frequently recurring attacks of vaginal candidosis. Such recurrent vulvo-vaginal candidosis (RVVC) is probably multifactorial in origin but one important factor might be a deficiency of T helper cell function. This is indicated by the close association of vaginal candidosis with HIV related immunodeficiency.^{1,2} Mendling and Koldovsky³ have suggested that healthy women with RVVC may have low peripheral blood T lymphocyte counts and that such low counts were predictive of a therapeutic response to Thymopentin. This study was performed to investigate whether, in otherwise healthy women, RVVC is associated with abnormalities of peripheral blood T lymphocyte subsets compared with a matched control group.

Subjects

Blood samples were taken from 26 unselected otherwise healthy women aged 22-39 years (mean age 30) attending the department of genitourinary medicine for treatment of RVVC. All had suffered at least four attacks of vaginal candidosis in the past year. At least three of these episodes had been proved by the isolation of a moderate or heavy growth of *Candida albicans* from a high vaginal swab. Control blood samples were taken from female clinical and laboratory staff, and patients with unrelated asymptomatic conditions from the department of genitourinary medicine—for example, as contacts of genital warts or non-gonococcal urethritis. Samples were matched

for time of day and age (within 5 years). Patients were offered an HIV test as part of their initial investigations but only three accepted this. They all proved HIV negative. Controls were not HIV tested. None of patients or controls admitted to any of the known risk factors for HIV. All patients were otherwise well and had no symptoms or history suggestive of a systemic medical condition.

Statistics

The sample size of at least 21 patients was chosen based on an assumed standard deviation of 250 cells $\times 10^6/l$ with a 90% power to exclude a difference of 250 cells $\times 10^6/l$ and $p < 0.05$.⁴ Although there was an attempt to pair controls with patients this was based on unpaired assumption so as to overestimate rather than underestimate the numbers required. Results from the control group were compared with the patient group by paired Student's *t* tests.

Laboratory methods

Blood samples were taken between 0800 and 1100 and processed within the hour. Absolute white cell counts were obtained using a Technicon 3H. The absolute lymphocyte count, T lymphocyte subsets, and B lymphocytes were measured in the regional immunology department. This is an accredited department which participates in a national quality assurance scheme. The method used was lysed whole blood staining and flow cytometry (Becton and Dickinson FACScan). The reagents were Dako fluorescein isothiocyanate or phycoerythrin conjugated CD14,

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Cell counts (cells × 10⁶/l) for patients and controls

	CD3		CD4		CD8		CD19	
	Control	Patient	Control	Patient	Control	Patient	Control	Patient
Mean	1295	1155	774	707	502	444	243	207
Median	1245	1130	755	700	495	405	245	210
Mean (± 2 SD)	1168 to 1422	1017 to 1293	691 to 857	553 to 860	424 to 580	370 to 518	205 to 281	179 to 235
Range	770 to 2280	610 to 2170	470 to 1320	360 to 1190	170 to 1100	210 to 950	60 to 500	70 to 350

45, 3, 4, 8, and 19. The gating reagent (CD45, 14) was used to ensure a purity of at least 95% lymphocytes in at least 95% of the total available lymphocytes with no monocyte contamination. Non-specific staining was defined with mouse isotypic control sera. The use of CD3, 4, and CD3, 8 reagent pairs ensured the exclusion of CD4 or CD8 non-T cells.

Results

The distribution of CD4 lymphocyte subset measurements in the patients and normal controls was very similar and there were no statistically significant differences between them (*t* = 1.15, *p* = 0.26). These results were similar to both the laboratory normal range and recently published reference range for HIV negative women.⁵ In addition, there was no significant difference between the cases and control groups with regard to CD3 (*t* = 1.31, *p* = 0.20), CD8 (*t* = 0.98, *p* = 0.34), or CD19 (*t* = 1.40, *p* = 0.17) lymphocyte subsets. Summary statistics for the differing groups are shown in the table.

Discussion

We were unable to find any significant difference between our patient group and the control group in levels of lymphocyte subsets as defined by CD3, CD4, CD8, and CD19 markers. Although there could be a small difference between the groups this is not at a level that is usually taken to be clinically significant—for example, in the context of HIV infection.

Recent work by Fidel *et al*⁶ demonstrated in a mouse model that T cell depletion did not alter the natural course of a primary vaginal

infection with *C albicans*. In a further paper by the same group⁷ the induction of *Candida* specific suppressor T cells had no effect on the vaginal *Candida* burden with the conclusion that, in this animal model, systemic Th-1 type cell mediated immunity was unrelated to protective events in the vaginal mucosa. In an animal model antibody mediated protection against candidal vaginitis has been demonstrated.⁸ Oral candidosis has been related in HIV infection to a loss of specific salivary antibody to *C albicans*.⁹ It may be therefore that the higher incidence of vaginal candidosis seen in HIV is related to secondary B cell dysregulation rather than T cell depletion itself.

Further work is required to delineate what if any deficit is present in the host defence mechanism of women suffering recurrent vaginal candidosis who are not infected by HIV. Any such deficit is not reflected by any clinically verifiable change of peripheral T cell subsets.

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